Listing of Claims:

Claims 1-23 (Canceled)

24. (New) A BMP antagonist with antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7 obtained by replacing at least one methionine or tryptophan residue existing in the receptor binding site of mature human MP52 (SEQ ID NO:1) with a hydrophilic amino acid residue or a polar amino acid residue, or converting said tryptophan residues to a hydrophilic residue by chemical modification.

25. (New) The BMP antagonist according to claim 24, wherein the chemical modification for said tryptophan residue is an allylsulphenylation reaction.

26. (New) The BMP antagonist according to claim 25 in which two tryptophan residues are allylsulphenylated and having the amino acid sequence of SEQ ID NO 7.

27. (New) The BMP antagonist according to claim 24, wherein said mature human MP52 is a dimer protein.

28. (New) A BMP antagonist with antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7 obtained by converting at least one residue of tryptophan residues existing in the amino acid sequences of mature human BMP-2 (SEQ ID NO 2), mature human BMP-4 (SEQ ID NO 3) or mature human BMP-7 (SEQ ID NO 4) to a hydrophilic residue by chemical

modification, or replacing said residues with a hydrophilic amino acid residue or a polar amino acid residue.

29. (New) A BMP antagonist with antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7 obtained by replacing at least one amino acid residue of three hydrophobic amino acid residues, among said hydrophobic amino acid residues relating to a receptor binding site in the amino acid sequences of mature human BMP-2 (SEQ ID NO 2), mature human BMP-4 (SEQ ID NO 3), or mature human BMP-7 (SEQ ID NO 4), which are located in positions corresponding to those of methionine residues located in 30th, 71st, and 74th positions of the amino acid sequence of mature human MP52 (SEQ ID NO 1) with a hydrophilic amino acid residue or a polar amino acid residue.

30. (New) The BMP antagonist according to claim 28, wherein said mature human BMP-2, mature human BMP-4, or mature human BMP-7 is a dimer protein.

31. (New) A therapeutic agent containing a BMP antagonist according to claim 24.

32. (New) A therapeutic agent for therapy of diseases due to the expression of MP52, BMP-2, BMP-4 and/or BMP-7 containing a BMP antagonist according to claim 24 as an effective ingredient.

33. (New) A BMP antagonist with antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7 obtained by converting at least one methionine residue existing in the receptor binding site of mature human MP52 (SEQ ID NO:1) by chemical modification, wherein said chemical modification for said methionine residue is an alkylation reaction.

34. (New) The BMP antagonist according to claim 33, wherein the alkylation reaction is S-carboxymethylation in which at least one methionine residue is S-carboxymethylated and having the amino acid sequence of SEQ ID NO 6.

35. (New) The BMP antagonist according to claim 33, wherein said mature human MP52 is a dimer protein.

36. (New) A therapeutic agent containing a BMP antagonist according to claim 33.

37. (New) A therapeutic agent for therapy of diseases due to the expression of MP52, BMP-2, BMP-4 and/or BMP-7 containing a BMP antagonist according to claim 33 as an effective ingredient.

38. (New) A method for antagonizing MP52, BMP-2, BMP-4 and BMP-7, comprising administering to a patient in need thereof, an effective amount of a mature modified protein according to claim 33.

39. (New) The method according to claim 38, wherein said patient is suffering from ectopic ossification which is due to ectopic expression of MP52, BMP-2, BMP-4 and/or BMP-7.

40. (New) The method according to claim 38, wherein said patient is suffering from a metabolic disease with calcification.

41. (New) The method according to claim 40, wherein said metabolic disease with calcification is calcification of arterial sclerosis.

42. (New) A mature modified protein obtained by replacing at least one methionine residue at position 30, 71 or 74 or at least one tryptophan residue existing in mature human MP52 (SEQ ID NO:1) with a hydrophilic amino acid residue or a polar amino acid residue, or converting said tryptophan residues to a hydrophilic residue by chemical modification, wherein said mature modified protein has antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7.

43. (New) A mature, modified protein obtained by replacing at least one methionine or at least one tryptophan residue existing in the receptor binding site of mature human MP52 (SEQ ID NO 1) with a hydrophilic amino acid residue or a polar amino acid residue, or converting said tryptophan residues to a hydrophilic residue by chemical modification, wherein said mature modified

protein has antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7.

44. (New) A method for antagonizing MP52, BMP-2, BMP-4 and BMP-7, comprising administering to a patient in need thereof, an effective amount of a mature modified protein according to claim 24.

45. (New) The method according to claim 44, wherein said patient is suffering from ectopic ossification which is due to ectopic expression of MP52, BMP-2, BMP-4 and/or BMP-7.

46. (New) The method according to claim 44, wherein said patient is suffering from a metabolic disease with calcification.

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47. (New) The method according to claim ~~47~~ 46, wherein said metabolic disease with calcification is calcification of arterial sclerosis.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

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David Romeo

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DSR
~~FEBRUARY 8, 2006~~

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March 28, 2006